Please amend claim 1 as follows:

1. (twice amended) A DNA segment consisting essentially of a sequence that encodes a human type α platelet derived growth factor receptor protein that preferentially binds the AA homodimer [form] and AB heterodimer forms of platelet derived growth factor and also binds the BB homodimer at high affinity.

In claim 5, line 1, delete "A" at the beginning of the sentence and substitute therefor --An *in vitro*--.

In claim 19, line 1, delete "A" and substitute therefor --An *in vitro*--.

REMARKS

Counsel for Applicants thank Examiner Marschel for the interview on July 9, 1992. The above amendments to claims 5 and 19, wherein "*in vitro*" is added to describe the claimed cultures, are in response to Examiner Marschel's suggestion made during that interview.

Claims 1-7 and 16-22 are pending. Applicants herewith cancel claim 17, without prejudice or disclaimer, and add claims 20-22. Thus, claims 1-7, 16 and 18-22 are active in this application.

Support for new claim 20 can be found, *inter alia*, in the specification at page 10, lines 4-15, wherein "HF1" is described and on page 20, lines 7-21, wherein the plasmid containing "HF1" (pHF1) is described. Further support can be found on page 36, line 21 to page 37, line 3 and in Figures 2 and 3.

Support for the amendment to claim 1 can be found in the specification at page 28, lines 9-23; page 47, line 1 to page 50, line 14; and at page 52, lines 4-21.

Issues related to 35 USC § 112

During the prosecution of the parent application and the interview, Examiner Marschel expressed some concern about the adequacy of the written description of pHF1 in the specification. Specifically, the Examiner has questioned how a skilled artisan could understand what is meant by pHF1, based upon the description in the specification and a combination of Figures 2 and 3. Although applicants welcome the opportunity to respond to these concerns, they point out that this issue has been rendered moot by the above amendment to the specification at page 36, line 26, wherein clone HF1 is described with reference to Figure 3, as beginning at nucleotide 2568 and continuing through the end of the full cDNA sequence. Applicants further assert that this amendment does not add new matter to the specification because this material merely further describes an inherent characteristic of the clone which was already described in the original disclosure.

However, in further response to the Examiner's concerns, applicants explain that in Figure 2, the first two lines represent the genomic T11 (Please refer to the attached copy of Figure 2). The first of these two lines represents the full genomic sequence; the second is an inset, or section of the full sequence. The third line, which is a solid bar, represents a cDNA clone of T11 called pHF1. The Examiner has stated that a discrepancy appears to arise when one aligns the KpnI site of the third line with that of the second line and then, based upon this information, attempts to locate this Kpn I site in the sequence of Figure 3. That is, based upon the location of the KpnI site

in Figure 3, which according to Figure 2 should be just to the 3' side of exon (b), pHF1 should also contain exon (a). However, the Examiner has expressed confusion because in Figure 2, the segment of the solid bar just 5' to the KpnI site in the third line is very short compared to the distance between the KpnI site and the beginning of exon (a) in the second line. The Examiner asks how it is possible that this short segment could fairly represent a sequence long enough to encompass exon (a) plus other nucleotides. Therefore, the Examiner questions the accuracy of Figure 2 in guiding a skilled artisan to pHF1 in Figure 3.

In response, applicants first point out that **the scale of the third line is different from the scale of the second line**, so that the segment of the third line just 5' of the KpnI site would be large enough to encompass exon (a) plus other nucleotide sequences. Applicants also again point out that the second line in Figure 2 represents genomic DNA which contains introns as well as exons, and that the third line represents cDNA which does not contain introns. Therefore, if one were to delete the section of the second line between the end of exon (a) and the beginning of exon (b), exons (a) and (b) would be adjacent to each other. In Figure 3, exons (a) and (b), in fact, **are** adjacent, so that Figure 2 can be easily reconciled with Figure 3. Moreover, the size of the section of solid bar on the third line just 5' of the KpnI site would be large enough to encompass exon (a). Thus, based upon the information provided by Figure 2, an artisan using routine interpretive skills could easily locate pHF1 in Figure 3 (starting at nucleotide 2568, specifically).

The Examiner also has questioned whether the relationship of pHF1 to TR4, as represented in Figure 2, is accurate in view of Figure 3. Specifically, the Examiner has noted that Figure 3 is the nucleotide sequence of TR4, the longest cDNA clone of genomic T11. The Examiner further has noted that pHF1 is a

fragment of TR4. According to Figure 2, the KpnI site shared by pHF1 and TR4 appears to fall just to the left of the center of the solid bar representing TR4. However, the Examiner asserts that the KpnI site in question does not appear to be located in a comparable position in Figure 3.

In response to the Examiner's question and in order to confirm the accuracy of Figure 2 in placing pHF1 in Figure 3, applicants have measured the full length of the TR4 solid bar in Figure 2, and the distance between the beginning of TR4 and the KpnI site on this solid bar. The length of the solid TR4 bar is approximately 11.5cm; the distance between the beginning of this bar and the KpnI site is approximately 5.25cm. If 6414 nucleotides are represented by an approximately 11.5cm long solid bar, then about 2928 nucleotides are represented by an approximate 5.25cm long bar. Although the actual KpnI site shared by TR4 and pHF1 is located at nucleotide 2879, the point of this exercise is to show that Figure 2 would have provided the skilled artisan with enough information to locate the approximate position of the pHF1 cDNA clone. Indeed, the difference between 2928 and 2879 represents less than a 2% error, well within scientific tolerance for errors, and arguably better than average for a schematic representation.

The Examiner also has asked applicants to provide the location of both KpnI sites in Figure 3 and the *Sac* I site shown in Figure 2 flanking the 3' side of exon (b) in the genomic clone. In response, applicants point out that the two KpnI sites (GGTACC) are located at nucleotides 645 and 2879 in Figure 3. Again, if one were to measure the solid bar representing TR4 in Figure 2, the distance between the first and second KpnI site would be approximately 4cm, representing about 2,231 nucleotides in Figure 3. If the first KpnI site is located at nucleotide 645, one would estimate that the second Kpn I site would be at

about nucleotide **2876** (645 + 2,231 = 2876). This estimate is unquestionably extremely close to the actual location of the second KpnI site at nucleotide **2879**.

Applicants further point out that the SacI site in the second line of Figure 2 cannot be found in Figure 3 because it is located in an intron which is not represented in Figure 3. Applicants reiterate that the second line of Figure 2 represents a genomic T11 clone which contains both introns and exons. Applicants' indication of the location of the two KpnI sites in Figure 3 should also resolve any confusion regarding the accuracy of Figure 2 in placing exons (a) (b) and (c).

Although applicants acknowledge that the interpretation of Figures 2 and 3 require certain skills and a good understanding of restriction maps and how they correlate with nucleotide sequence listings, such skills and knowledge is routine to the skilled artisan of the present invention. Indeed, exercises such as the above are a matter of routine to the skilled artisan. Therefore, applicants assert that Figures 2 and 3 either alone or in conjunction with the description in the specification, provide an adequate written description of pHF1 under the law.

However, because the Examiner has repeatedly expressed skepticism about the accuracy of Figures 2 and 3, applicants have amended the specification to set forth the exact nucleotides where pHF1 can be found in the sequence of Figure 3. As discussed above, the specification has been amended to read that pHF1 begins at nucleotide 2568 and continues to the end of the full sequence of Figure 3. Applicants reiterate that this information does not constitute new matter because it merely further characterizes what was inherently disclosed in the application as originally filed. Thus, no new matter has been added with this amendment.

Applicants mention that they have also amended the specification in order to further describe pHF1 as having American Type Culture Collection Accession No. 75058.

New claim 20

New claim 20 is directed to isolated DNA which hybridizes under stringent conditions with polynucleotide encoding α platelet derived growth factor receptor protein. During the interview, the Examiner indicated that claim 20 might be objectionable because, theoretically, "any DNA could hybridize with polynucleotide encoding α platelet derived growth factor receptor protein, including the poly-a tail." In anticipation of a rejection along these lines, applicants wish to explain that the Examiner's concerns are unfounded. Indeed, claim 20 requires that hybridization occur **under stringent conditions.** In further response, and in accordance with the Examiner's suggestion, applicants have further described the isolated DNA as one that hybridizes under stringent conditions with a polynucleotide encoding human α platelet- derived growth factor receptor protein **but not β platelet-derived growth factor receptor protein.**

Deposit Issues

Applicants have deposited plasmid pHF1 and pH851 at the ATCC. The specification has been amended to reflect these deposits. Plamid pHF1 is claimed in claims 21 and 22. Plasmid pH851, on the other hand, contains a nucleotide sequence which hybridizes with polynucleotide encoding β platelet derived growth factor receptor protein and represents subject matter which is not covered by the present claims.

The undersigned representative of the Applicants, having the designated registration number, states that plasmids pHF1 and

pH815 have been deposited with the American Type Culture Collection under the terms of the Budapest Treaty and will be irrevocably and without restriction or condition released to the public upon issuance of a patent in this case.

Miscellaneous

In the Official Action, the Examiner stated at page 2, third full paragraph, that "[t]he amendment filed 7/23/91 has been entered. . . but that the deletions on pages 73-88 were difficult to understand since these correspond to pages of drawings but were not labeled as such in the amendment." In response to the Examiner's concern, applicants confirm that the designated pages are correct and that these pages contain drawings, the captions for which have been deleted with the 7/23/91 amendment. Indeed, the line numbers referred to in the amendment correspond to the text of the various drawing captions.

On page two, in paragraph 4 of the Official Action, the Examiner requests applicants to submit a new Abstract containing a description of "the DNA compositions" claimed. In response to this request, applicants submit the attached Abstract which conforms to U.S. Patent Office practice.

CONCLUSION

Counsel for applicants again thank Examiner Marschel for the courtesy of an interview. In light of the above explanations, amendments and statement with regard to deposits under the Budapest Treaty, applicants assert that the specification and claims meet every requirement under § 112 and that claims 1-7, 16 and 18-22 are in condition for allowance. Early notification thereof is earnestly solicited. Examiner Marschel is invited to contact the undersigned at (703) 836-9300

to discuss any matters related to this case.

Respectfully submitted,

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August 27, 1992

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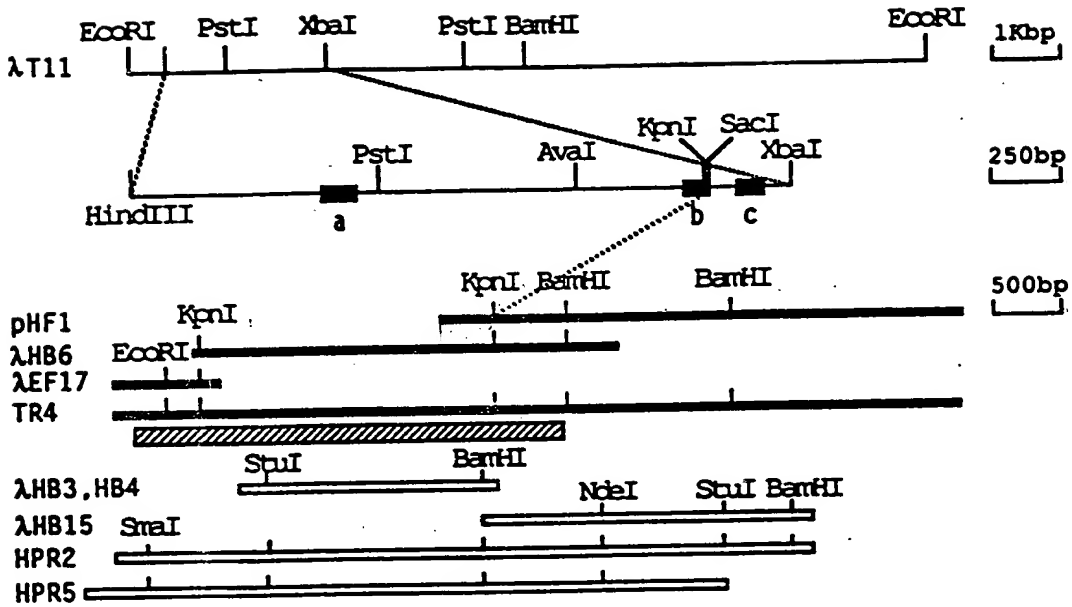

Figure 2. Molecular cloning of the λT11 genomic fragment as well as cDNAs of T11 and PDGF-R genes. Restriction map of: λT11 genomic clone (solid lines); T11 cDNA clones (solid bars); and PDGF-R cDNA clones (open bars). Coding regions within three fragments, as determined by nucleotide sequencing analysis, are indicated by black boxes labeled a, b and c.